REMARKS

Claims 1-21, 25-29, 72, and 83-88 were pending in the application. Claims 3, 4, 8, 27, 72, 83 and 86 have been amended. Claims 22-24, 30-71 and 73-82 have been canceled without prejudice. Upon entry of this amendment, claims 1-21, 25-29, 72 and 83-88 will be pending.

The claims amendments do not present new issues requiring further consideration or search. The amendments also present the claims in better form in case of appeal (37 C.F.R. § 1.116 (b)). Therefore, Applicants respectfully request the entry of the amendments.

No new matter has been added.

Rejection under 35 U.S.C. § 101

Claims 1-21, 25-29, 72 and 83-88 remain rejected under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by a specific, substantial and credible asserted utility or a well established utility. The Office alleges that the arguments presented by Applicants in response to the previous Office Action, although considered, were not deemed persuasive. Applicants disagree and request reconsideration of the rejection.

The Utility Examination Guidelines (the "Guidelines") require that a claimed invention have a specific, substantial and credible asserted utility, or, alternatively a well-established utility. As Applicants have asserted utilities that are specific, substantial and credible, and well established, the Utility Requirement has been satisfied. Applicants therefore respectfully request the withdrawal of the rejection under 35 U.S.C. § 101.

Under the Guidelines, Office personnel are instructed to review the specification and claims of the application to determine if a specific and substantial utility that is credible is present. The Guidelines note that the specific and substantial requirement "excludes 'throw-away', insubstantial,' or 'nonspecific' utilities, such as the use of a complex invention as landfill." The Guidelines go on to note that an Examiner's "*prima facie* showing ***must*** establish that it is more likely than not that a person of ordinary skill

in the art would not consider that nay utility asserted by the applicant would be specific and substantial." "If the applicant has asserted that the claimed invention is useful for any particular practical purpose (*i.e.*, it has a 'specific and substantial utility') and the assertion would be considered credible by a person of ordinary skill in the art, do ***not*** impose a rejection based on lack of utility." (Guidelines, emphasis added).

The Guidelines also comment on the use of computer based analysis of nucleic acids to assign functions to a nucleic acid or polypeptide based upon homology to sequences found in databases. Specifically, the Guidelines state that the:

> suggestions to adopt a *per se* rule rejecting homology based assertions of utility ***are not adopted***. An applicant is entitled to a patent to the subject matter claimed unless statutory requirements are not met (35 U.S.C. 101, 102, 103, 112) . . .The inquiries involved in assessing utility are fact dependent, and the determinations must be made on the basis of scientific evidence. Reliance on the commenters' *per se* rule, rather than a fact dependent inquiry, is impermissible because the commenters provide no scientific evidence that homology-based assertions of utility are inherently unbelievable or involve implausible scientific principles. *See, e.g., In re Brana,* 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (rejection of claims improper where claims did 'not suggest an inherently unbelievable undertaking or involve implausible scientific principles' and where ''prior art * * * discloses structurally similar compounds to those claimed by the applicants which have been proven * * * to be effective').
>
> A patent examiner ***must*** accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. The examiner's decision must be supported by a preponderance of all the evidence of record. *In re Oetiker,* 977 F.2d 1443, 1445, 24 USPQ2d 1443,1444 (Fed. Cir. 1992). More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. ''[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient.'' *Fujikawa* v. *Wattanasin,* 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996). The Office will take into account both the nature and degree of the homology.
>
> When a class of proteins is defined such that the members share a specific, substantial, and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial, and credible utility to the assigned protein. If the

> preponderance of the evidence of record, or of sound scientific reasoning, casts doubt upon such an asserted utility, the examiner should reject the claim for lack of utility under 35 U.S.C. 101. For example, where a class of proteins is defined by common structural features, but evidence shows that the members of the class do not share a specific, substantial functional attribute or utility, despite having structural features in common, membership in the class may not impute a specific, substantial, and credible utility to a new member of the class. When there is a reason to doubt the functional protein assignment, the utility examination may turn to whether or not the asserted protein encoded by a claimed nucleic acid has a well-established use. If there is a well-established utility for the protein and the claimed nucleic acid, the claim would meet the requirements for utility under 35 U.S.C. 101. If not, the burden shifts to the applicant to provide evidence supporting a well-established utility. There is no *per se* rule regarding homology, and each application must be judged on its own merits.

(Guidelines; emphasis added).

Preliminarily, Applicants remind the Office that specific and substantial utilities have been provided for the claimed polypeptides. The asserted utilities are credible to one of skill in the art. The Office has failed to provide any evidence that "it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial."

It appears that the Examiner's assertion that the claimed invention lacks utility may have been based upon the often-repeated examples of "throwaway" utilities, including the use of a genetically modified mouse as snake food or of the use of uncharacterized compositions as "landfill" or as shampoo ingredients. Such assertions focus on the non-specificity of such uses. For example, anything that a snake could arguably fit within its mouth could serve as food for the snake. Likewise, anything that could fit in a landfill could be a landfill component. Virtually any substance that can be dissolved in a shampoo could be used a shampoo ingredient. An important issue raised by the fact that any substance could be so used is that the substance may be wholly inappropriate for the asserted utility. In the context of a shampoo ingredient, the added substance may be highly caustic and cause serious burns to the skin. This scenario supports the logical conclusion that such a substance should be appropriate for the utility asserted. Further, to be "appropriate for use", the substance cannot be uncharacterized.

Without characterization one cannot determine whether the substance is appropriate for the asserted utility.

The use of such uncharacterized substances for purposes of dubious worth stands in sharp contrast to the present invention. As recited in Applicants' previous response, the pending claims recite a ***specific*** polypeptide, *i.e.*, nGCPR-2037. Through several rounds of analysis, the claimed polypeptide was shown to be a GPCR. Applicants note that the claimed sequence is not an olfactory GPCR (*see* page 59, paragraph [000234]). The polypeptide was further shown to be related to the human and rodent galanin receptor (*see* paragraph page 63 of the application as filed, lines 3-8). Applicants note that the expression profiles of nGPCR-2037 are similar to those of the galanin receptor. The nucleotide and amino acid sequences of nGPCR-2037 are provided as SEQ ID NO:1 (nucleotide) and SEQ ID NOS:2-3 (amino acid). Specific expression profiles for the nGPCR-2037 polypeptide are provided in Example 5. Such polypeptides are useful, *inter alia*, for generating antibodies, identifying ligands or protein partners, evaluating expression patterns, evaluating protein activity, etc. As set forth in Example 5, the claimed polypeptides also:

> have utility for treating neurological disorders, including but not limited to, movement disorders, affective disorders, metabolic disorders (including obesity and diabetes), endocrine disorders, as well as inflammatory disorders and cancers. Use of nGPCR-2037 modulators, including nGPCR-2037 ligands and anti-nGPCR-2037 antibodies, to treat individuals having such disease states is intended as an aspect of the invention.

It is clear therefore the claimed polypeptide is neither the equivalent of the uncharacterized complex invention used as "landfill" nor of the caustic substance used in a shampoo.

Galanin receptors, receptors to which the claimed polypeptides have been shown to share sequence homology, are known to activate K+ channels by coupling to G proteins of the Gi/Go class (Brancheket al., Trends Pharmacol. Sci. 21(3) 109-117 (2000)). Galanin is a neurotransmitter in the peripheral and central nervous systems. In the peripheral nervous system, galanin inhibits glucose-induced insulin release and is thought to be the sympathetic mediator of this effect during stress. In the CNS, galanin inhibits

firing of locus coeruleus cells, is synergistic with opiates in inducing analgesia at the level of the spinal cord. Galanin also and stimulates feeding behavior and release of growth hormone. The ability of galanin to inhibit acetylcholine release in the hippocampus has led to the suggestion that galanin antagonists may be of use, *inter alia*, in the treatment of Alzheimer's disease.

As indicated by the Guidelines, the assignment of the claimed polypeptide to the galanin receptor family imputes the same specific, substantial, and credible utility to the claimed polypeptide. The Examiner has failed to provide any evidence, less still a preponderance of the evidence, to cast doubt upon any of the asserted utilities.

Applicants further note that the Office has already acknowledged the close relationship between the claimed invention and the galanin family of receptors. In the Office Action mailed March 21, 2003, the Office cited Elshourbagy *et al.* (U.S. Patent Application Publication US 2001/0016337) as prior art. In Applicants' response to the March 21, 2003 Office Action, Applicants pointed out that the Elshourbagy *et al.* reference was not available as prior art against the present application. Notably the Elshourbagy *et al.* reference discusses nucleotides and polypeptide sequences that "show homology with Human Galanin Receptor." (Elshourbagy *et al.*, paragraph [0047]). Applicants respectfully assert that, as set forth in the specification and as acknowledged by the Office, several utilities have been provided for the claimed invention based on its close homology to the galanin receptor. The Office has failed to provide any evidence that the members of the galanin class do ***not*** share a specific, substantial functional attribute or utility.

The Examiner compares the claimed invention to, *inter alia*, a "molecular weight marker/calibration standard", or a source of heat or light through combustion. The Examiner goes on to say that "to accept Applicant's arguments that any nucleic acid encoding any protein of human origin is useful as a marker would be comparable to conceding that any object of fixed mass has *prima facie* utility as a weight standard, irrespective of any other properties possessed by that object." Also, the Office alleges that if Applicants' assertions were followed, "any item having a constant mass within an

acceptable range can be used to calibrate a produce scale in a grocery store" and that this was "irrespective of any other properties possessed by that object." (Office Action, page 4).

As discussed above, the Office, through its analogy, appears to imply that the claimed polypeptides are wholly unsuitable for the asserted utilities; i.e. because wholly unsuitable objects ***could*** be used for purposes not specific to the object. For example, ***anything*** could be used to calibrate a grocery scale. Applicants agree that there are numerous objects which ***could*** be used to calibrate a grocery scale but, for any number of reasons, many of such objects may be inappropriate or unsuited for that utility. Applicants note, however, that the Office has failed to provide any reason why the claimed polypeptides are inappropriate or unsuited for the several asserted utilities. Applicants remind the Examiner that the utilities asserted for the claimed polypeptide are not "irrespective of any other properties possessed by that object."

Applicants again note that the claimed invention has substantial and specific utilities that are credible, in contrast to the use of any (even uncharacterized) objects as calibration standards. Notwithstanding the Office's arguments regarding unsubstantial or nonspecific utilities of calibration standards, *inter alia*, Applicants assume, however, that the Office recognizes that objects including calibration standards, ***when appropriate for use***, are patentable. Indeed, upon a cursory review of patents listed on the PTO's website, Applicants found numerous patents issued with claims directed to, *inter alia*, calibration standards. For example, United States Patent 6,646,737, issued November 11, 2003, claims a calibration standard. Similarly, United States Patents 6,356,069 and 6,174,728 also claim calibration standards. Applicants have provided evidence, including several different homology comparisons and expression analysis, that the claimed polypeptides are suitable for use as GPCRs, and, more specifically, as galanin receptors.

The Office further makes the assertion that granting Applicants:

> a patent encompassing an isolated polynucleotide encoding a naturally occurring human protein of as yet undetermined biological significance, or the protein encoded thereby, would be to grant Applicant a monopoly 'the metes and bounds' of which 'are not capable of precise delineation.' That monopoly 'may engross a vast, unknown, and perhaps unknowable area' and

> 'confer power to block off whole areas of scientific development, without compensating benefit to the public.

(Office Action, page 5 (citing *Brenner v. Manson*)).

Applicants respectfully assert that the Office has mischaracterized the *Brenner* decision. Applicants first note that the pending claims are not directed to processes but instead to compositions. The Office apparently failed to consider the entirety of first sentence cited from Brenner. The sentence in its entirety states "Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation." The equivalent of the "product" discussed in Brenner is the claimed polypeptide. As discussed in length above, many utilities have been asserted for the claimed polypeptides. None of the asserted utilities are incredible or have dubious worth.

Further, Applicants note that rejections of claims based on the "metes and bounds" of the claim are properly made under 35 U.S.C. § 112, second paragraph. Applicants respectfully assert that the art-skilled would readily comprehend the "metes and bounds" of the presently claimed nGPCR-2037 polypeptides.

Applicants note that only a "substantial likelihood" of utility need be provided; certainty is not required. *Brenner*, 383 U.S. at 532. The amount of evidence required to prove utility depends on the facts of each particular case. *In re Jolles*, 628 F.2d 1322, 1326 (CCPA 1980). "The character and amount of evidence may vary, depending on whether the alleged utility appears to accord with or to contravene established scientific principles and beliefs." *Id.* Unless there is proof of "total incapacity," or there is a "complete absence of data" to support the applicant's assertion of utility, the utility requirement is met. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 (Fed. Cir. 1992); *Envirotech*, 730 F.2d at 762. The Office has failed to provide proof of "total incapacity". Applicants have provided data that supports the asserted utilities. Accordingly the utility requirement has been met.

Although Applicants assert that specific and substantial utilities that are credible have been provided for the claimed invention, Applicants also note that the Utility requirement may also be satisfied by an "Art Established Utility" which means that "a

person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention . . . and the utility is specific, substantial and credible." (M.P.E.P. §2107). Well-established, art established utilities exist for the claimed polypeptides of the present invention.

To support Applicants assertion that there is an "Art Established Utility," Applicants point out that commercial products relating to GPCRs for which no ***confirmed*** function has been identified are commercially available. GPCRs, ORF clones of GPCRs, and antibodies that bind to GPCRs are commercially available. For example, Applicants points out that FabGennix Inc. of Shreveport, Louisiana sells an antibody directed to Retinal Anti-GP75. GPCR75 is said to be a GPCR for which a ligand has not yet been identified (*see* attached product sheet). Invitrogen sells ORF clones of GPCRs including those for which a ligand has not yet been identified (*see* attached list, especially noting Clone Ids IOH22483, IOH14039, IOH13056, IOH22637, IOH13239, and IOH13516). MD Bio of Taiwan sells GPCR peptides and antibodies against such peptides, again where no ligand has yet been identified. That at least three companies make and sell such GPCR products proves that there is an art-established utility for the presently claimed GPCR polypeptides. Applicants note that it is an industry standard to develop such products before confirmation of a function. Accordingly there could be no better proof of the utilities of the claimed polypeptides- such products are made by a manufacturer (who expects to sell them) for consumers (who expect to buy them). Any argument that there is no art-recognized utility for such polypeptides, and the polynucleotides that encode them, seems meritless. If the Patent Office is aware of any evidence which would support the Office substituting its judgment for the practices of the industry, Applicants respectfully request that an affidavit stating the basis of this evidence be placed on the record.

In summary, a patent examiner ***must*** accept a utility asserted by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. The Guidelines make clear that when a patent application claiming a nucleic acid, for example, asserts a specific, substantial, and credible utility, and bases the assertion upon

homology to existing nucleic acids or proteins having an accepted utility, the asserted utility ***must*** be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. The Office has failed to provide any evidence, less still a preponderance of the evidence, to cast doubt upon any of the asserted utilities. The Office has also failed to provide any evidence that the asserted utilities are "throwaway utilities" or that the claimed polypeptides are inappropriate or unsuited for the several asserted utilities. Finally, even assuming *arguendo* that the asserted utilities are not specific or substantial, the art established utilities for the claimed polypeptides satisfy the Utility requirement of § 101.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn upon reconsideration.

Rejections under 35 U.S.C. § 112

Claims 1-21, 25-29, 72, 83 and 88 remain rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to adequately teach how to use the instant invention.

As discussed above, the present invention ***is*** supported by a specific, substantial, and credible asserted utility as well as a well-established utility. Accordingly, Applicants respectfully request that the rejection be withdrawn.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

Claims 72, 83 and 86-88 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly vague and indefinite. The Office alleges that the phrase "'stringent hybridization conditions' is conditional and neither the claims nor the instant specification identified a single set of conditions that define this limitation." (Office Action, page 7). Applicants respectfully disagree.

The phrase "stringent hybridization conditions" is well known to the art skilled and, as acknowledged by the Office, is defined in the instant specification.

Notwithstanding the foregoing, however, Applicants have amended claims 72 and 86 to incorporate the specific hybridization conditions set forth in the claims as originally filed.

The Office alleged that claim 72 was "confusing in the recitation of the phrase 'a polynucleotide encoding comprising the amino acid sequence.'" (Office Action, page 7). Claim 72 has been amended to correct this typographical mistake.

The Office alleged that claim 73 "is confusing in so far as it refers to 'a sequence of SEQ ID NO:1' because there only appears to be one sequence in SEQ ID NO:1." (Office Action, page 7). Although Applicants assert that the skilled artisan would readily understand the cited language, Applicants have amended claims 2, 3 and 8 to further clarify the claim language.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

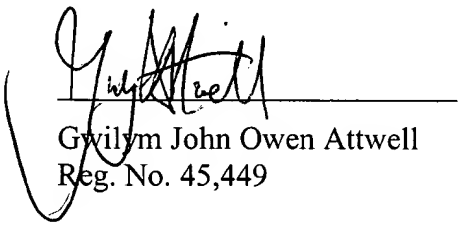
Withdrawn Claims

The Office notes that the instant application contains withdrawn claims directed to non-elected inventions and requires cancellation of the withdrawn claims. Applicants have canceled the claims previously withdrawn without prejudice to future presentation in related applications.

Conclusion

Applicants believe the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-6904 to clarify any unresolved issues raised by this response.

Respectfully submitted,



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Date: **December 29, 2003**

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Attachments: Product Sheet for Anti-GPCR-75 Antibodies
Product sheet for GPCR control peptides and antibodies (MD Bio)
Product sheet for GPCR ORF clones (Invitrogen)
Brancheket al., Trends Pharmacol. Sci. 21(3) 109-117 (2000)